

April 12, 1954

Lawrence L. Weed
North Broadway
Baltimore 5
Maryland

Mr. Larry:

Thank you for sending me the letter from Clark. However I think it would be quite inappropriate for me to answer it directly. I will take the occasion to let you know the current status of our work on the problem.

A Miss Helen Byers has been concerning herself almost exclusively with this story since the beginning of the present academic year. She has had considerable difficulty in reproducibly repeating your results, but has more recently found a rather curious correlation between colonial morphology and susceptibility to copper at various sublines of the strain B. Our main interest in the problem is, of course, to ascertain the genetic bases of the copper effect. So far, Miss Byers has not been able to obtain any evidence of a direct induction by copper. She has secured a detectable yield of small colony variance only with treatments that decimated the exposed populations. A few of her attempts to repeat your briefly mentioned experiment of exposing very small numbers of cells to copper have failed completely; the cultures have either been completely sterilized, or at lower copper concentrations there was no effect whatsoever. If you have any suggestions on how we might find better luck in following your result in this important experiment I would be indebted to you for them.

In E. coli K-12, the results of copper treatments have been much more erratic, and I am not yet convinced that an analogous mutation occurs in that strain. A few small colony types can of course be isolated but these have a much less characteristic appearance than do the variants from strain B and at best occur in only a sporadic fashion. Miss Byers will also be surveying a number of other potentially crossable strains for what may prove to be more satisfactory material for breeding experiments. She has also done a few crosses with the so-called small colony variants of K-12 and these have indicated only a typical genetic mutation as the basis of the growth defect.

We had not ourselves intended to do anything by way of a cytological or a cytochemical study on this situation until the genetic angle was cleared up. I see no reason whatsoever why you should not comply with Dr. Clark's request but it would be most discreet of course if you could convey to him the fact of Miss Byer's interest in the problem. If he would then like to pursue the matter further directly with me, it would be of course more than appropriate for him to write me directly.

I have been a little concerned about the significance of nucleic acid ratios in the variant in that these ratios have a distinct dependence on the growth phase of the culture. The small colony variant obviously follows a different course for its growth in time. I do not know how one could more precisely correlate the phases of the two kinds of culture. Had you noticed, in this connection, the paper by Beljanski which appeared in the Annales of the Pasteur Institute for October 1953? He reports that

April 12, 1954

mutants resistant to streptomycin become richer in RNA and poorer in DNA.

Entirely aside from all this I have hoped that I could still persuade you to consider a nucleic acid analysis of normal and small colony yeast. If my persuasion can have any chance of being effective, I will be happy to send you representative cultures at your own convenience.

I realize how preoccupied you must be at the present time, but will look forward to hearing from you at greater length perhaps when you have taken up your scientific work again at Yale.

Yours sincerely,

Joshua Lederberg

img

cl.